Asian J Gerontol Geriatr 2020;15(2):66–73 | https://doi.org/10.12809/ajgg-2019-380-oa

Incidence and risk factors for delirium in older patients with hip fracture

ORIGINAL ARTICLE

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ABSTRACT

Introduction. Delirium is a common complication of hip fracture that can be avoided or ameliorated by careful anticipatory case management. We aimed to investigate the incidence and risk factors of delirium in older patients with hip fracture treated in our structured integrated care unit, and to evaluate the impact of delirium on healthcare utilisation.

Methods. We retrospectively reviewed records of patients aged ≥60 years and admitted to our unit from December 2014 to September 2018 with low-impact hip fracture. Our unit has implemented a structured integrated care programme based on the NICE guidelines. Primary outcome measure was the incidence of delirium. The diagnosis of delirium was established using the Confusion Assessment Method. Secondary outcome measures included length of hospital stay, readmission within 30 days of discharge, and mortality within 30 days and 1 year.

Results. A total of 1304 patients were included and classified as non-delirium (349 men and 815 women; mean age, 79.2 years) and delirium (49 men and 91 women; mean age, 82.3 years). The overall within-episode incidence of delirium was thus 10.7%. Independent risk factors for delirium in older patients with hip fractures were age (odds ratio [OR]=1.028, p=0.02), surgical treatment (OR=2.202, p=0.006), dementia (OR=2.066, p=0.001), elevated body temperature (OR=1.966, p=0.001), urinary tract infection (OR=2.431, p<0.001), and acute coronary syndrome (OR=4.587, p<0.001). Those with delirium had prolonged hospitalisation of ≥10 days (OR=2.033, p<0.001) and higher mortality within 30 days (OR=3.408, p=0.002) and 1 year (OR=1.894, p=0.004).

Conclusion. The incidence of delirium was low in the present study, compared with most studies. The structured integrated care programme in our unit enables early recognition of delirium for prevention and management of delirium in older patients with hip fracture and might contribute to better outcomes.

Key words: Aged; Delirium; Health care costs; Hip fractures

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INTRODUCTION

The population of Singapore is expected to grow from 5.7 million to 6.6 million between 2017 and 2050,[1] by which time about 40% of Singaporeans are expected to be aged >60 years.[2] Hip fracture is likely to be a major public health issue for this increasingly ageing population. In economically advanced countries, the lifetime risk of hip fracture is typically about 11% for men and 23% for women, with almost half of all

hip fractures occurring in those aged ≥80 years.[3] Hip fracture in older people results in an increased risk of mortality, impaired quality of life, and persistent physical morbidity. In Singapore, in 2013, the 1-year mortality rate after a fragility hip fracture was approximately 20% to 27%. Furthermore, 20% of such patients remained partially or fully dependent, around 40% had reduced mobility, and an increasing proportion lived in an institutionalised home.[4,5]

In the United States, 48% of patients with hip fracture aged ≥65 years had a degree of delirium before, during, or after surgery.[6] Delirium is a severe neuropsychiatric syndrome that is common and serious in older patients with hip fracture. It is often under-recognised and undertreated, and can occur at any time during the course of hip fracture episode.[7,8] Delirium can unravel a cascade of adverse outcomes that have significant implications for patients and their families, with a substantial impact on healthcare utilisation and costs. Delirium causes prolonged hospitalisation,[9] delayed rehabilitation efforts,[10,11] poorer functional outcomes and cognitive function,[10] increased risk of nursing home placement,[12,13] and increased mortality after hip fracture.[13,14] Delirium is associated with high rates of mortality both in hospital and after discharge, especially for those who underwent surgery.[15-17] Delirium is also associated with the development of dementia,[3] although it is unclear whether delirium is a marker of undetected dementia or whether delirium contributes to the development of dementia, or both.[13]

Although the aetiology of delirium in older patients with hip fracture is usually multifactorial, reduced cognitive reserve appears to be an important predisposition. According to the National Institute for Health and Care Excellence (NICE),[18] the five major risk factors associated with postoperative delirium are age >65 years, chronic cognitive decline or dementia, poor vision or hearing, severe comorbid illness (affecting activity of daily living), and the presence of infection. Of these, age is the most significant predictor.[18-21]

A review of 25 studies categorised risk factors of delirium into predisposing and precipitating factors. The former include age, male sex, cognitive impairment, functional impairment, sedentary lifestyle, major comorbidity such as cardiovascular disease, congestive cardiac failure, depression, and polypharmacy (>3 prescribed drugs). The latter include laboratory abnormalities such as anaemia and disturbed electrolytes, depression, and drugs, particularly opioids and anticholinergics.[21]

Other studies have suggested associations between delirium and malnutrition, sensory (vision and hearing) impairment, history of cerebrovascular disease, endocrine disease, prolonged waiting time for operation, type of fracture, type of anaesthesia, inadequate analgesia, elevated temperature, pneumonia, and urinary tract infection; however, none has shown clear single associations. In clinical practice, these factors appear to be contributary to multifactorial delirium.[21-31]

Therefore, a better understanding of these factors is useful in attempts to identify patients at high risk of developing delirium and hence devising effective preventive and management strategies.

The present study aimed to determine the incidence and risk factors of delirium in the Geriatric Hip Fracture Unit at Khoo Teck Puat Hospital, Singapore, where a structured integrated care programme was developed and implemented in 2014 using the NICE guidelines. We also aimed to evaluate the impact of delirium on healthcare utilisation as measured by length of hospital stay, readmission to hospital within 30 days of discharge, and mortality within 30 days and 1 year.

METHODS

Approval for the study was obtained from the Institutional Ethics Review Board of Singapore (reference: 2015/00661). We retrospectively reviewed a prospectively collected database that comprise all patients who were admitted to the Geriatric Hip Fracture Unit at Khoo Teck Puat Hospital, Singapore from December 2014 to September 2018 for treatment of hip fracture. The inclusion criteria were patients aged ≥60 years with a principal diagnosis of accidental low-impact hip fracture (neck of femur, inter-trochanteric fracture or subtrochanteric fracture within 5 cm of the lesser trochanter). Exclusion criteria were newly diagnosed acute stroke, pathological hip fracture, high-impact hip fracture, or multiple lower-limb fractures.

The structured integrated care programme in our

unit included admission within 4 hours to a general ward from the emergency department, surgery within 4 hours of being ready for an operation, early delirium screening, active early optimisation of comorbidities by collaboration with multiple specialties including geriatric medicine, anaesthesia, and, if necessary, with cardiology and other medical specialties. From shortly after admission, corrective attention was given to nutrition, fluids and electrolytes, pain management, urinary tract infection prevention, venous thromboembolism prevention (with subcutaneous low-molecular-weight heparin unless contra-indicated), rehabilitation as early as possible, and active prevention of postoperative complications (if surgery was performed).

The baseline clinical characteristics collected recorded were: age, sex, ethnicity, comorbidities, Charlson comorbidity index, abbreviated mental test (AMT) score, type of fracture and the management options (surgical vs conservative), and the time taken for transfer from the emergency department to a general ward. Clinical data were extracted in patients who developed anaemia requiring blood transfusion, elevated body temperature, presence of urinary tract infection, hospital-acquired pneumonia, wound- or catheter-related infection, deep vein thrombosis, pulmonary embolism, acute cerebrovascular accident, and acute coronary events.

The diagnosis of delirium was established using the Confusion Assessment Method, which provides a standardised evidence-based tool to identify and recognise delirium quickly, effectively, and accurately in both clinical and research settings.[32] As part of the structure integrated care programme, the Confusion Assessment Method was initiated in the emergency department and continued daily until postoperative day 4 (if the patient underwent surgery) by a trained geriatric nurse and geriatricians, respectively. It takes account of (1) acute onset and/or fluctuation, (2) inattention, (3) disorganised thinking, and (4) altered level of consciousness. The diagnosis of delirium requires the presence of features 1 and 2 and either 3 or 4. The secondary outcomes measured included length of hospital stay, readmission within 30 days, and mortality within 30 days and 1 year.

Statistical analysis was performed using SPSS (Windows version 22.0; IBM Corp, Armonk [NY], US). Continuous data were analysed by an independent samples t-test. Categorical variables were described as percentages and analysed by either the Chi-squared test or Fisher's exact test, depending on the sample size. Univariate logistic analysis was used to identify the risk factors associated with delirium in older patients with hip fracture. The variables identified as significant, with the exception of low AMT score, were subsequently included in a stepwise multivariate logistic analysis to identify independent predictors of delirium. A p value of <0.05 was considered statistically significant. Low AMT score was not included in the multivariate logistic analysis because a large proportion of AMT data were missing (221 patients, 16.9%).

RESULTS

A total of 1304 patients were included from December 2014 to September 2018. The non-delirium group comprised 1164 patients (349 men and 815 women; mean age, 79.2±8.8 years) and the delirium group 140 patients (49 men and 91 women; mean age, 82.3±8.1 years). The overall within-episode incidence of delirium was thus 10.7%.

Univariate logistic analysis revealed that delirium in older patients with hip fracture was associated with age (odds ratio [OR]=1.041, $p<0.001$), Charlson comorbidity index (OR=1.123, p=0.009), chronic obstructive pulmonary disease (OR=5.076, p=0.027), ischaemic heart disease (OR=1.865, p=0.005), chronic kidney failure (OR=2.684, p=0.001), thyroid disorders (OR=8.42, p=0.034), dementia (OR=2.283, $p<0.001$), low AMT score of <8 (OR=2.577, $p<0.001$), elevated body temperature (OR=2.417, $p<0.001$), urinary tract infection (OR=3.06, $p<0.001$), hospital-acquired pneumonia (OR=3.358, $p<0.001$), and acute coronary syndrome (OR=5.09, $p<0.001$). In addition, delirium was associated with prolonged hospitalisation of ≥10 days (OR=2.033, $p<0.001$), and mortality within 30 days (OR=3.408, p=0.002) and 1 year (OR=1.894, p=0.004) [Table 1].

Multivariate analysis showed that independent risk factors for delirium in older patients with hip fractures were age (OR=1.028, p=0.02), surgical treatment (OR=2.202, p=0.006), dementia (OR=2.066, p=0.001), elevated body temperature (OR=1.966, p=0.001), urinary tract infection (OR=2.431, $p<0.001$), and acute coronary syndrome (OR=4.587, $p<0.001$) [Table 2].

Table 1
Patient characteristics and outcome of the delirium and non-delirium groups and univariate analysis for risk factors of delirium in older patients with hip fracture

Variables	Delirium group (n=140)*	Non-delirium group (n=1164)*	p Value	Unadjusted odds ratio (95% confidence interval for exp (B))	p Value
Age, y	82.3±8.1	79.2±8.8	<0.001	1.041 (1.02-1.063)	<0.001
Age group, y			<0.001		
60-69	11 (5.6)	187 (94.4)		1	
70-79	37 (8.6)	393 (91.4)		1.601 (0.799-3.208)	0.185
80-89	64 (12.5)	446 (87.5)		2.439 (1.258-4.73)	0.008
≥90	28 (16.9)	138 (83.1)		3.449 (1.66-7.167)	0.001
Sex			0.223		
Male	49 (12.3)	349 (87.7)		1.257 (0.869-1.1819)	0.224
Female	91 (10.0)	815 (90.0)		1	
Ethnicity			0.296		
Chinese	106 (10.3)	921 (89.7)		1	
Malay	26 (14.5)	153 (85.5)		1.477 (0.93-2.343)	0.098
Indian	6 (8.7)	63 (91.3)		0.827 (0.35-1.958)	0.667
Others	2 (6.9)	28 (93.1)		0.644 (0.151-2.745)	0.551
Type of fracture			0.506		
Intertrochanteric	69 (11.4)	538 (88.6)		1	
Neck of femur	66 (9.9)	598 (90.1)		0.861 (0.602-1.23)	0.41
Subtrochanteric	5 (15.2)	28 (84.8)		1.392 (0.52-3.725)	0.51
Management			0.144		
Surgery	119 (11.4)	929 (88.6)		1.433 (0.882-2.329)	0.146
Non surgery	21 (8.2)	235 (91.8)		1	
Charlson comorbidity index	5.76±1.67	5.33±1.83	0.009	1.123 (1.029-1.226)	0.009
Comorbidities					
Hypertension	98 (10.9)	804 (89.1)	0.822	1.045 (0.713-1.531)	0.822
Hyperlipidaemia	72 (11.4)	562 (88.6)	0.482	1.134 (0.799-1.611)	0.482
Diabetes mellitus	42 (9.7)	392 (90.3)	0.383	0.844 (0.576-1.236)	0.383
Asthma	7 (15.2)	39 (84.8)	0.318	1.518 (0.666-3.462)	0.321
Chronic obstructive pulmonary disease	3 (37.5)	5 (62.5)	0.014	5.076 (1.2-21.472)	0.027
Ischaemic heart disease	31 (16.8)	154 (83.2)	0.004	1.865 (1.209-2.877)	0.005
Chronic heart failure	1 (7.7)	12 (92.3)	0.722	0.691 (0.089-5.352)	0.723
Chronic kidney failure	17 (23.0)	57 (77.0)	<0.001	2.684 (1.514-4.76)	0.001
End stage renal failure	0	3 (100)	0.548		
Liver cirrhosis	1 (50.0)	1 (50.0)	0.073	8.367 (0.52-134.514)	0.134
Anaemia	16 (11.0)	130 (89.0)	0.927	1.026 (0.591-1.782)	0.927
Thyroid disorder	2 (50.0)	2 (50.0)	0.011	8.42 (1.177-60.252)	0.034
Stroke	10 (8.8)	104 (91.2)	0.478	0.784 (0.4-1.538)	0.479
Parkinsonism	2 (33.3)	4 (66.7)	0.073	4.23 (0.763-23.157)	0.099
Malignancy	0	1 (100)	0.729		
Dementia	45 (18.4)	200 (81.6)	<0.001	2.283 (1.552-3.359)	<0.001
Abbreviated mental test score			<0.001		
<8	84 (14.7)	488 (85.3)		2.577 (1.682-3.946)	<0.001
≥8	32 (6.3)	479 (93.7)		1	

* Data are presented No. (%) of cases or mean±standard deviation

Table 1 (cont'd)

Variables	Delirium group (n=140)*	Non-delirium group (n=1164)*	p Value	Unadjusted odds ratio (95% confidence interval for exp (B))	p Value
Door to admission			0.471		
≤4 hours	51 (11.7)	385 (88.3)		1	
>4 hours	88 (10.4)	760 (89.6)		0.874 (0.606-1.26)	0.471
Complication					
Anaemia requiring transfusion	79 (12.1)	573 (87.9)	0.107	1.336 (0.938-1.902)	0.108
Elevated body temperature	89 (15.4)	488 (84.6)	<0.001	2.417 (1.681-3.477)	<0.001
Urinary tract infection	42 (22.7)	143 (77.3)	<0.001	3.06 (2.048-4.572)	<0.001
Hospital-acquired pneumonia	19 (26.8)	52 (73.2)	<0.001	3.358 (1.922-5.866)	<0.001
Wound infection	4 (23.5)	13 (76.5)	0.086	2.604 (0.837-8.099)	0.098
Catheter-related infection	0	3 (100)	0.548		
Acute coronary syndrome	21 (35.0)	39 (65.0)	<0.001	5.09 (2.899-8.94)	<0.001
Pressure ulcer	1 (33.3)	2 (66.7)	0.206	4.18 (0.377-46.394)	0.244
Deep vein thrombosis	3 (15.0)	17 (85.0)	0.535	1.477 (0.428-5.106)	0.537
Pulmonary embolism	0	11 (100)	0.248		
Stroke	1 (16.7)	5 (83.3)	0.637	1.668 (0.193-14.377)	0.642
Length of stay, d	15.1±11.6	12.3±8.4	0.005	1.027 (1.011-1.042)	0.001
<10	53 (7.6)	645 (92.4)	<0.001	1	
≥10	87 (14.3)	520 (85.7)		2.033 (1.418-2.915)	<0.001
Readmission within 30 days	15 (13.4)	97 (86.6)	0.342	1.32 (0.743-2.345)	0.344
Mortality within 30 days	9 (28.1)	23 (71.9)	0.001	3.408 (1.544-7.521)	0.002
Mortality within 1 year	31 (16.9)	152 (83.1)	0.003	1.894 (1.227-2.922)	0.004

Table 2
Multivariate analysis for independent risk factors of delirium in older patients with hip fracture

Variable	Unadjusted odds ratio (95% confidence interval for exp (B))	p Value
Age	1.028 (1.004-1.052)	0.02
Sex	1.390 (0.922-2.097)	0.116
Surgical treatment	2.202 (1.254-3.865)	0.006
Charlson morbidity index	1.013 (0.896-1.145)	0.837
Ischaemic heart disease	1.569 (0.957-2.573)	0.074
Chronic obstructive pulmonary disease	4.480 (0.931-21.560)	0.061
Chronic kidney disease	1.724 (0.883-3.366)	0.111
Thyroid disorder	6.472 (0.829-50.514)	0.075
Dementia	2.066 (1.335-3.198)	0.001
Elevated body temperature	1.966 (1.314-2.942)	0.001
Anaemia requiring transfusion	0.953 (0.643-1.413)	0.812
Urinary tract infection	2.431 (1.560-3.790)	<0.001
Hospital-acquired pneumonia	1.802 (0.968-3.356)	0.063
Acute coronary syndrome	4.587 (2.473-8.508)	<0.001

DISCUSSION

Delirium is an important complication of hip fractures in older patients and has considerable implications for healthcare utilisation, care costs, and mortality risk. The incidence of delirium in our Geriatric Hip Fracture Unit was 10.7%, which is substantially lower than the 13% to 62% reported by most other studies.[14,33-35] Although some of this variation is likely to be due to differences in case mix and definitions, we contend that our low delirium incidence might in part be due to the structured integrated care programme, with early detection and amelioration of risk factors, timely optimisation of patients' physiological status, and application of the NICE delirium guideline. This is consistent with the established evidence that comprehensive geriatric assessment and care reduces the incidence of perioperative delirium across a range of surgical conditions, as demonstrated by meta-analysis of randomised controlled trials.[14,33,34] The low incidence of delirium in our unit could also have been partly due to the use of the Confusion Assessment Method, which can underdiagnose mild hypoactive delirium.[32] Our study had neither a parallel nor a preceding control group for comparison of the delirium incidence, so caution is needed when ascribing the low incidence to the structured integrated care. Nevertheless, anecdotal evidence from clinicians supported our interpretation of the benefit of the structured integrated care programme.

There is no high-grade evidence of benefit from specific treatments for established delirium. Therefore, identifying and correcting the risk factors for delirium are the most effective means to reduce the incidence of delirium. This concords with the finding that in the general geriatric population, 30% to 40% of the delirium episodes could be prevented by better management of the risk factors.[34]

In the present study, independent risk factors for delirium in older patients with hip fracture were age >80 years, surgical treatment, dementia, elevated body temperature, and presence of urinary tract infection and acute coronary syndrome. This concords with other studies in which advanced age was consistently an independent risk factor for delirium in older patients with hip fracture, and the risk rises incrementally with increasing age.[18-20,27] Similarly, our study established that age was not only an independent risk factor for delirium but also that the incidence of delirium in patients aged 80-89 years (OR=2.439, 95% CI=1.258-4.73, p=0.008) and >90 years (OR=3.449, 95% CI=1.66-7.167, p<0.001) was higher than that in patients aged <80 years. Age is confirmed as the major non-modifiable risk factor for delirium in patients with hip fracture.

Older patients are more susceptible to delirium because of the association between ageing and depleted physiological reserves leading to impaired compensatory capability to adjust to the physical stress of surgery. Older patients generally also have significant neurovascular risk factors, higher white matter vascular damage, and less cognitive reserve; all of which predispose them to a higher risk for cognitive complications in physically stressful circumstances such as hip fracture.[33-35]

The other main non-modifiable risk factor is dementia. Patients with dementia have greatly reduced cognitive reserves as a result of structural alteration and neurotransmitter dysfunction. They frequently have other comorbidities, functional dependency, and poor nutritional state.[33] In our study, patients with dementia were >2 times more likely to develop delirium than patients with normal cognition. The increased risk of delirium in dementia patients is consistent with other studies, and confirms it as a major risk factor for delirium in older patients with hip fracture.[21]

In older patients with hip fracture, those treated operatively were more susceptible to the development of delirium than those managed conservatively. General anaesthesia and surgical trauma have been shown to cause disturbances to a wide variety of neurotransmitters systems and that is the most likely substrate for their proneness to delirium. Our study demonstrated that patients treated surgically were >2 times more likely to develop delirium than those treated conservatively.

Elevated body temperature and the presence of urinary tract infection were independent risk factors of delirium in our older patients with hip fracture. These findings concorded with the NICE delirium clinical guideline, which highlighted presence of infection as one of the major risk factors for delirium. There is increasing evidence to suggest that trauma, infection, and surgery can lead to increased

production of proinflammatory cytokines,[30] which can induce delirium in susceptible individuals.[31] High levels of cortisol associated with acute stress might be a factor; patients with postoperative delirium were found to have high cortisol levels after surgery.[36] The physiological feedback regulation of cortisol might be impaired in older adults resulting in higher levels of baseline cortisol and thereby predisposing them to delirium, although a causative relationship has not been confirmed. A similar mechanism might be at work in patients with hip fracture with acute coronary syndrome who are likewise prone to delirium. Acute coronary syndrome has been reported to be strongly independently associated with delirium.[34,35] A full discussion of the biochemical mechanisms of delirium are outside the scope of this paper.

These findings of our study have practical implications for management of older patients with hip fracture during hospitalisation. The benefit of the structured integrated care indicates that patients at high risk should be monitored closely and consistently for early signs of delirium. Delirium in our sample was associated with increased length of hospital stay and increased mortality within 30 days and 1 year after hip fracture. Delirium inevitably has a profound impact on healthcare utilisation. With the rising proportion of the population at risk of fragility hip fracture, the implications of delirium are substantial from clinical and health services perspectives.

Our study has some limitations. First, there was no clear record of when in the episode the delirium was detected. It was unknown whether it was pre-, peri- or post-operative. There was also no record of the severity or subtype of delirium to help to refine the approach to prevent and manage delirium in older patients with hip fracture. Second, the history of cognitive impairment or dementia was evaluated using medical notes. No distinction was made between mild, moderate, and severe cognitive impairment. In addition, dementia often became apparent for the first time at admission; this may have underestimated the number of patients with dementia. Third, data pertaining to AMT scores were incomplete and this may have resulted in false positive results in some patients. Fourth, the dataset was not sufficient to adjust for all confounders known to influence the development of delirium. Despite these limitations, our study provided useful information to improve our understanding of the incidence and risk factors of delirium in older patients with hip fracture. We contend that our findings are generalisable and could help other hospitals to develop and implement effective strategies to reduce the incidence of delirium and to improve management.

CONCLUSION

Independent risk factors for developing delirium in older patients with hip fracture were age, dementia, surgical treatment, elevated body temperature, urinary tract infection, and acute coronary syndrome. Delirium was associated with prolonged hospitalisation and increased morbidity and mortality. The structured integrated care programme in our unit enables early recognition of delirium for prevention and management of delirium in older patients with hip fracture and might contribute to better outcomes.

DECLARATION

The authors have no conflict of interest to disclose.

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